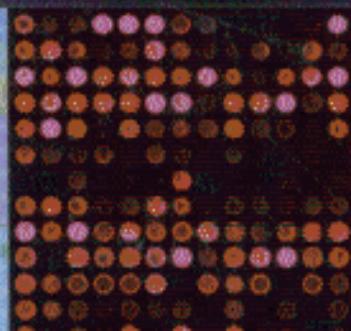


GENOMICS PROTEOMICS and VACCINES

Editor
GUIDO GRANDI



Contents

Preface	xi
List of contributors	xix
PART 1: INTRODUCTION	
1 Vaccination: Past, Present and Future	3
<i>Maria Lattanzi and Rino Rappuoli</i>	
1.1 Introduction	3
1.2 Vaccination: the past	4
1.3 Vaccination: the present	6
1.4 Vaccination: the future	12
1.5 Conclusion: the intangible value of vaccination	14
References	15
2 Bioinformatics, DNA Microarrays and Proteomics in Vaccine Discovery: Competing or Complementary Technologies?	23
<i>Guido Grandi</i>	
2.1 Introduction	23
2.2 From genome sequence to vaccine discovery	25
2.3 A case study: the anti-meningococcus B vaccine	28
2.4 Comparison of the three approaches	34
2.5 Conclusions: a ‘omics’ approach to vaccine discovery	37
References	40

PART 2: TECHNOLOGIES

3	Genome Sequencing and Analysis	45
<i>Hervé Tettelin and Tamara Feldblyum</i>		
3.1	Introduction	45
3.2	Genome sequencing	46
3.3	Genome analysis	60
3.4	Conclusion	65
	References	65
4	Understanding DNA Microarrays: Sources and Magnitudes of Variances in DNA Microarray Data Sets	75
<i>She-pin Hung, Suman Sundaresh, Pierre F. Baldi and G. Wesley Hatfield</i>		
4.1	Introduction	75
4.2	DNA array formats	76
4.3	Data analysis methods	79
4.4	Sources and magnitudes of noise in DNA microarray experiments	84
4.5	Conclusions	97
	Acknowledgements	100
	References	100
5	The Proteome, Anno Domini Two Zero Zero Three	103
<i>Pier Giorgio Righetti, Mahmoud Hamdan, Frederic Reymond and Joël S. Rossier</i>		
5.1	Introduction	103
5.2	Some definitions	105
5.3	What methods exist to tackle the proteome complexity?	107
5.4	Quantitative proteomics	112
5.5	Pre-fractionation in proteome analysis	117
5.6	Multi-dimensional chromatography	120
5.7	Protein chip arrays	123
5.8	Imaging mass spectrometry	126
	Acknowledgements	127
	References	127

6	Mass Spectrometry in Proteomics	135
<i>Pierre-Alain Binz</i>		
6.1	Introduction	135
6.2	MS technology	136
6.3	Principle of protein identification based on MS data	147
6.4	Proteomics workflows	155
	References	155
7	High Throughput Cloning, Expression and Purification Technologies	171
<i>Andreas Kreusch and Scott A. Lesley</i>		
7.1	Introduction	171
7.2	Gene cloning	172
7.3	Protein expression	174
7.4	High-throughput protein purification	175
7.5	Validation of the pipeline and outlook	178
7.6	Conclusion	179
	References	180
PART 3: APPLICATIONS		
8	Meningococcus B: from Genome to Vaccine	185
<i>Davide Serruto, Rino Rappuoli and Mariagrazia Pizza</i>		
8.1	Meningococcus, a major cause of bacterial meningitis	185
8.2	Group B meningococcus as an example of reverse vaccinology	190
8.3	Conclusions	200
	References	201
9	Vaccines Against Pathogenic Streptococci	205
<i>John L. Telford, Immaculada Margarit y Ros, Domenico Maione, Vega Massignani, Hervé Tettelin, Giuliano Bensi and Guido Grandi</i>		
9.1	Introduction	205
9.2	Comparative genomics of streptococci	206
9.3	A vaccine against group B streptococcus	208
9.4	A vaccine against group A streptococcus	215
9.5	Conclusions	218
	References	219

10	Identification of the ‘Antigenome’ – a Novel Tool for Design and Development of Subunit Vaccines Against Bacterial Pathogens	223
	<i>Eszter Nagy, Tamás Henics, Alexander von Gabain and Andreas Meinke</i>	
10.1	Introduction	223
10.2	Small DNA insert libraries – a tool to cover a pathogen’s ‘antigenome’	227
10.3	Proper display platforms	230
10.4	Selected human sera to provide imprints of pathogen encounters	231
10.5	Cognate antibodies reveal the ‘antigenome’ of a pathogen	234
10.6	How to retrieve from the ‘antigenome’ the candidate antigens for vaccine development	235
10.7	Summary and discussion	237
	References	239
11	Searching the Chlamydia Genomes for New Vaccine Candidates	245
	<i>Giulio Ratti, Oretta Finco and Guido Grandi</i>	
11.1	Old problems and new perspectives for chlamydial vaccines	245
11.2	Post-genomic approaches	250
11.3	Genomic screening results	251
11.4	Concluding considerations	262
	References	263
12	Proteomics and Anti-Chlamydia Vaccine Discovery	267
	<i>Gunna Christiansen, Svend Birkelund, Brian B. Vandahl and Allan C Shaw</i>	
12.1	Introduction	267
12.2	Proteome analysis	269
12.3	Proteomics as a complement for genomics	277
12.4	Benefits that proteomics provide for vaccine development	279
	References	280
13	Proteome Analysis of Outer Membrane and Extracellular Proteins from <i>Pseudomonas aeruginosa</i> for Vaccine Discovery	285
	<i>Stuart J. Cordwell and Amanda S. Nouwens</i>	
13.1	Introduction	285

CONTENTS

ix

13.2	Membrane proteins in <i>P. aeruginosa</i>	286
13.3	Extracellular proteins in <i>P. aeruginosa</i>	292
13.4	Immunogenic proteins and vaccine discovery	296
13.5	Conclusions	298
	References	299

Index

305